

## REMARKS

The courtesies extended by Examiner Anne Kubelik to Applicants' representatives, Allan Fanucci and Rodney Fuller, during the interview on June 18, 2003 are noted and appreciated. The comments and amendments presented herein are substantially the same as those that were presented and discussed at the interview.

Claims 56-57 are cancelled herein. Claims 47, 49, 51, 58, 60, 62, 64-66, 68, 73-76 are amended herein. Claims 47, 49, 51, 58, 60, 62-79 are presently pending. The amended claims are supported by the specification and original claims so that their entry at this time is warranted. No new matter is being introduced. Specifically, the amendments to claims 47 and 49, directed to the step of introducing a polynucleotide sequence are supported in the specification, for example at page 17, lines 32-42 and page 23, lines 17-29. Furthermore, the amendment to claims 47, 49 and 51, directed to the phenotype of the resulting offspring being male sterile is supported by the specification, for example, at page 8, lines 4-6 and page 23, lines 35-37; the amendments to claims 58 and 60, by Example 2 of the specification, at page 27, lines 31-32; and the amendment of claim 65 and 74 by page 14, lines 41 thru page 15, line 2.

Claims 59 and 61 were objected to for the reasons set forth on page 2 of the Office Action. Claims 59 and 61 have been cancelled herein, so that the reasons for objection are no longer applicable.

Claims 59, 61, 64, and 73 were objected to for the reasons set forth on pages 2-3 of the Office Action. Claims 59 and 61 have been cancelled herein, so that the reasons for objection are no longer applicable and claims 64 and 73 have been amended to replace the missing article.

Claims 47, 49, 51 and 55-79 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement for the reasons set forth on pages 3-5 of the Office Action. Applicants traverse.

The Examiner's first reason for the rejection is that the claims are drawn to "introducing a recombinase into a plant by topical application" and that the specification does not enable topical application of recombinase. Applicants have amended claims 47 and 49 to resolve this misunderstanding. It was never the intention of Applicants to attempt to topically apply the recombinase protein to the subject plant. The amendments to the claims reflect this point and are fully supported by the specification, for example, at page 17, line 38 to page 18, line 6 and by the Examples on pages 25-27, wherein the specification teaches that the polynucleotide sequence that encodes a recombinase is introduced into the plant by use of

transformation techniques or preferably by cross-fertilization (sexual crosses) with a plant known to carry an active recombinase. Applicants provided support of enablement for both of these techniques in the March 20, 2003 response, including a PowerPoint presentation and Declaration of Dr. Vered Yesodi.

The second reason given by the Examiner for the rejection is that the "specification does not teach transformation of a plant with a RNA molecule or a transactivator that is non-operable with eukaryotic promoters" and further argues that the "[t]ransformation with RNA would not result in integration of the exogene into the plant."

Applicants do not intend to transform a plant with an RNA molecule or a transactivator. Applicants have amended the claims to reflect this point and to resolve any further misunderstandings the Examiner may have. Claims 64 and 73 have been amended to require that the exogene encodes an RNA molecule and claims 65 and 74 to delete the phrase "transactivator that is non-operable with eukaryotic promoters."

The final reason the Examiner gives for the enablement rejection is that the specification "does not teach gene combinations suitable for exogenic allelism other than those involved in making male sterile plants." Applicants emphatically traverse this rejection for all of the reasons previously stated in the March 20, 2003 response.

In an effort to expedite the allowance of these claims, however, Applicants have amended independent claims 47, 49 and 51 to require that the offspring obtained not only be characterized by exogenic allelism, but also by male sterility, wherein the expression of the first and the second transcribable polynucleotide sequences results in male sterility of the plant.

While, Applicants have amended the claims as suggested by the Examiner, so that this rejection is now moot, Applicants wish to point out that the specification does provides examples of exogenic allelism with other phenotypes other than just male sterility, for example, at page 13, lines 18-24, (plants with differential resistivity to pathogens and chemicals, differentiated development and the like); at page 24, lines 21-28 (using exogenic allelism to express equal-molar amounts of two distinct exogenes); and at page 6, lines 16-21, (commercially important products). Based on the present specification, one skilled in the art would understand that exogenic allelism can be used to express many phenotypes, wherein the phenotype is advantageous for a hybrid, but its expression in the following generation is not desirable, for example a genetically modified plant bearing pesticide or herbicide resistance, wherein there is concern regarding leakage of modified genes to the environment.

In view of the foregoing, the presently claimed invention is fully enabled. Applicants therefore respectfully request that this rejection be withdrawn.

Claims 47, 49, 51 and 55-79 were rejected under 35 U.S.C. §112, first paragraph, for lack of written description for the reasons set forth on pages 5-6 of the Office Action. Applicants traverse.

Again, in an effort to expedite the allowance of the claims Applicants have amended the claims to recite that the offspring obtained be characterized by exogenic allelism, wherein the expression of the first and the second transcribable polynucleotide sequences results in male sterility of the plant.

Such a plant and method of producing it is fully described by the specification, for example at pages 19-20 and by Examples 1 and 2.

Finally, claims 65 and 74 have been amended to delete the phrase "transactivator that is non-operable with eukaryotic promoters" to expedite the allowance of the claims.

Applicants have met the written description requirement by describing each and every step of the presently claimed methods in the specification (see pages 7, 12-24), by providing specific examples of how to use the method (see Examples 1 and 2; Figures 1 and 2), and by providing detailed examples of specific implementations of the presently claimed method. And the Examiner has not cited any evidence or document that would cast doubt on the efficacy of the presently claimed method. Accordingly, one skilled in the art would reasonably conclude that the inventors had possession of the presently claimed methods of generating plants characterized by exogenic allelism and the plants produced by these methods.

In view of the amendments and the above statements, Applicants respectfully request that this rejection be withdrawn.

Claims 47, 49 and 56-79 were rejected under 35 USC §112, second paragraph, as being indefinite.

The Examiner states that claim 47, part (c), and claim 49, parts (b) and (c), are indefinite in the recitation of "having the expression cassette wherein the third segment has been excised." Applicants have amended claims 47, part (c) and claim 49, parts (b) and (c) to state, in relevant part, ". . . wherein the progeny comprises the expression cassette in which" the segment has been excised.

Claims 58 and 60 were rejected for being indefinite in the recitation of "characterized by exogenic allelism." Claims 58 and 60 have been amended as suggested by

the Examiner, to clarify that the plant or the plant seed is characterized by exogenic allelism and not the method.

Claims 64 and 73 were rejected as being indefinite for the recitation of "wherein the first exogene is RNA molecule." Claims 64 and 73 have both been amended to clearly set forth that the exogene encodes an RNA molecule.

Claims 65 and 74 were rejected for being indefinite in their recitation of the phrase, "transactivator non-operable with eukaryotic promoters." Claims 65 and 74 have been amended to delete the term "transactivator non-operable with eukaryotic promoters."

In view of these amendments, Applicants respectfully request that the rejections for indefiniteness be withdrawn.

Claims 58-59 were rejected under 35 USC §102(e) as being anticipated by U.S. Patent No. 6,392,119 to Gutterson *et al.* (referred to hereafter as "Gutterson"). The rejection is also repeated for the reasons of record as set forth in the Office Action mailed 22 October 2002, as applied to claims 47, 50, and 55-56. Applicants traverse.

Claims 50, 55-56 and 59 have been cancelled. Only claims 47 and 58 remain rejected under 35 U.S.C. §102(e). Presently amended claim 47 is directed to a method of generating exogenic allelism in a plant. The method specifically requires the step of "selecting a progeny devoid of said recombinase" prior to the step of "crossing the plant obtained from the selection step with said second plant . . . ." As pointed out in the June 18, 2003 Interview, Gutterson does not disclose or teach the step of selecting a progeny devoid of recombinase. Applicants' invention provides the added benefit of increased reliability, preventing sequence shuffling in the desired progeny. Without some teaching in Gutterson of this essential active selection step, it cannot anticipate Applicants' invention.

In order for a prior art reference to anticipate a claimed invention, the reference must teach every aspect of the claimed invention. Gutterson fails to teach each and every step of Applicants' invention and therefore it cannot anticipate the invention as presently claimed. Claim 58 is dependent from claim 47 and therefore is also is not anticipated.

In view of the foregoing, Applicants respectfully request that the anticipation rejection based on Gutterson be withdrawn.

Claims 47, 56, 58-59 and 62-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,392,119 to Gutterson *et al.* (referred to hereafter as "Gutterson") for the reasons set forth on pages 8-10 of the Office Action.

Examiner states that although Gutterson does not teach the step of "selecting a selfed progeny that lacks recombinase[,] . . . it would have been obvious to one of ordinary skill in the art to modify the method of generating exogenic allelism as taught by Gutterson *et al.*, to select a selfed progeny that lacks recombinase." The Examiner goes on to say that "[o]ne skilled in the art would have been motivated to do so because one skill [sic] in the art would know that the presence of the recombinase in the selfed progeny would mean that when the selfed progeny is backcrossed to the first plant, the resulting progeny would be subject to the action of the recombinase and progeny with exogenic allelism would not be produced." Applicants traverse this rejection.

The Examiner is correct that there is no teaching in Gutterson of selecting for progeny that lack recombinase. Applicants further point out, that not only does Gutterson not teach, Applicants' presently claimed method with the selection step, but Gutterson does not even suggest such a step or the necessity of it. Furthermore, the art at the time Applicants' invention was made actually taught that the recombinase gene should be selected for, in contrast to Applicants' disclosure. This is evidenced by the art cited by the Examiner in the previous Office Actions, for example, Gidoni *et al.* at page 154, left Col., Para. 2; Qin *et al.* at page 1706 and Golic *et al.* at page 252.

It was Applicants' present disclosure that taught the need and value of the additional step of actively selecting for progeny devoid of recombinase. The Examiner's conclusion of obviousness therefore appears to be based on improper hindsight reasons. The Federal Circuit has expressly prohibited the use of hindsight as a substitute for the requirement that the references provide a motivation to make such alterations.

While the presently claimed invention may seem obvious to the Examiner now, in light of Applicants' disclosure, at the time the invention was made there was no teaching or suggestion by Gutterson, or any other reference, of the presently claimed method at the time Applicants' invention was made. Without some teaching or suggestion in the prior art of the need to modify the method Gutterson, one skilled in the art would also not be motivated to modify the method disclosed in Gutterson as suggested by the Examiner. To modify the Gutterson method as suggested by the Examiner, would incurring additional cost and time to analyze each plant to determine whether it is devoid of the recombinase gene prior to the final crossing step. There is no such motivation in Gutterson or the art to do. As pointed out above, the cited references previously provided by the Examiner showing the state of the art at the time the invention was made actually teach that one should select for the presence of recombinase, contrary to Applicants' invention, further providing support for the

fact that Applicants' invention was not obvious at the time it was first made. With no teaching or suggestion in Gutterson, or other prior art, Applicants invention cannot be found to be obvious over Gutterson.

In order to make a proper obviousness rejection, there must first be some suggestion or motivation to modify the reference. Second, there must be some reasonable expectation of success in the prior art and "not based on applicant's disclosure." And finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). As Gutterson fails to teach or suggest all of the steps of the presently claimed invention and further fails to provide any suggestion or motivation to modify the method disclosed in Gutterson in the way suggested by the Examiner, Gutterson cannot make obvious the presently claimed invention.

In view of the foregoing, Applicants respectfully request that this obviousness rejection be withdrawn.

If the Examiner would find it helpful, Applicants can also provide the Examiner with a Declaration by a skilled artisan declaring that the presently claimed method is not obvious, and specifically, that step (c) of Applicants' invention, selecting a progeny devoid of recombinase, would not be obvious to one skilled in the art in view of Gutterson at the time the invention was made without the use of hindsight. If such a declaration would be helpful to the Examiner, please let our representatives know at your earliest convenience so that we can promptly provide you with a copy.

In addition, Applicants point out that the limitation of dependent claims 65 and 66 are also not taught or suggested by Gutterson. Dependent claim 65 is directed to the method of claim 47, wherein the expression product of the first exogene transactivates the expression of the second gene. Gutterson does not teach or suggest such an expression product. Claim 66 is dependent from claim 65 and list specific transactivators.

Applicants appreciate the Examiner acknowledgement that Claims 49, 51, 57, 60-61, and 71-79 are free of the prior art.

In view of the foregoing, it is believed that the entire application is now in condition for allowance, early notice of which would be appreciated. Should any issues remain, a personal or telephonic interview is respectfully requested to discuss the same in order to expedite the allowance of all the claims in this application.

Respectfully submitted,

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Date

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